

AMENDMENTS TO THE CLAIMS

1. (Currently amended) A method for generating antigen-binding fragments of an antibody, comprising:

providing an antibody-producing cell line that is growing in a cell media under conditions to express antibodies;

adjusting ~~the pH~~ conditions of the cell media to activate at least one endogenous enzyme in said cell media that cleaves said antibodies, ~~wherein the adjusted conditions are selected from the group consisting of temperature conditions and pH conditions;~~ and

incubating said cell line under said adjusted pH conditions so that said antibodies are cleaved into antigen-binding antibody fragments.

2. (Original) The method of Claim 1, wherein said antibodies are cleaved into F(ab')₂ fragments.

3. (Currently amended) The method of Claim 1, further comprising ~~wherein adjusting the conditions of the cell media comprises~~ adjusting the temperature conditions of the cell media.

4. (Canceled)

5. (Currently amended) The method of Claim 4 1, wherein adjusting the pH conditions comprises adjusting ~~the a pH of the cell media~~ to about pH 3.5.

6. (Original) The method of Claim 1, further comprising inactivating said at least one endogenous enzyme after incubating said cell line.

7. (Previously presented) The method of Claim 1, further comprising substantially purifying said antigen-binding antibody fragments by affinity chromatography.

8. (Original) The method of Claim 1, wherein said at least one enzyme comprises a serine protease.

9. (Original) The method of Claim 1, wherein said at least one enzyme comprises a cysteine protease.

10. (Original) The method of Claim 1, wherein said at least one enzyme comprises an aspartyl protease.

11. (Original) The method of Claim 1 wherein the cell line comprises cells selected from the group consisting of: Chinese hamster ovary cells, HeLa cells, baby hamster kidney cells, monkey kidney cells, and human hepatocellular carcinoma cells.

12. (Canceled)

13. (Currently Amended) The method of Claim 1 wherein the cell line is provided in media is a protein free media.

14. (Currently Amended) The method of Claim 1 wherein the cell line is provided in a media comprises comprising a peptone source.

15. (Currently Amended) The method of Claim 1 wherein the cell line is provided in media is a CD-CHO media.

16. (Currently amended) The method of Claim 1 further comprising inactivating said at least one enzyme by adjusting a pH of the cell media.

17. (Original) The method of Claim 16 wherein inactivating said at least one enzyme comprises inactivating a cysteinyl enzyme.

18. (Original) The method of Claim 17 further comprising activating an aspartyl enzyme by adjusting the pH of the cell media after endogenous cysteinyl enzyme activity has been reduced.

19. (Currently amended) A method for producing F(ab')₂ fragments of an antibody, comprising:

providing a cell media comprising a cell line that is growing under conditions to produce a recombinant antibody;

inactivating endogenous cysteinyl enzyme activity in said cell media; and

activating endogenous aspartyl enzyme activity in said cell media, ~~wherein said activation~~ by adjusting pH conditions of the cell media, such that said activating results in cleavage of said recombinant antibody into F(ab')₂ fragments.

20. (Currently amended) The method of Claim 19 wherein the cell line is provided in media is a CD-CHO media.

21. (Currently amended) The method of Claim 19, wherein inactivating endogenous cysteinyl enzyme activity comprises adjusting ~~the~~ a pH of the cell media.

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22. (Original) The method of Claim 19, wherein inactivating endogenous cysteinyl enzyme activity comprises adding a cysteinyl enzyme inhibitor to the cell media.

23. (Currently amended) The method of Claim 22, wherein said cysteinyl enzyme inhibitor is E64.

24. (Canceled)

25. (Original) The method of Claim 19, further comprising purifying said $F(ab')_2$ fragments from said cell media.

26 – 29. (Canceled)